Journal of the American College of Cardiology Vol. 45, No. 6, 2005

Published by Elsevier Inc.
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2004.12.021

EDITORIAL COMMENT

Echocardiographic Findings and the Search for a Gold Standard in Patients With Arrhythmogenic Right Ventricular Dysplasia*

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The proper diagnosis of patients with arrhythmogenic right ventricular dysplasia (ARVD) remains an important problem. This is due to the fact that, unfortunately, no gold standard exists for making the diagnosis of ARVD. As such, we rely on Task Force criteria for making this diagnosis (1). Although the Task Force criteria are of value in allowing different investigators to use a set of homogeneous criteria, they are clearly imperfect as a true gold standard. Conformity does not necessarily mean accuracy.

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A positive diagnosis is made with presence of two major, one major and two minor, or four minor criteria. A close look at the criteria reveals flaws in practical application. For example, minor right ventricular (RV) wall-motion abnormalities are considered a minor criterion, but this involves subjective interpretation of what constitutes "mild." So, for example, a patient who has "mild" RV wall-motion abnormalities, sustained left bundle branch block ventricular tachycardia (minor), and inverted T waves in electrocardiographic leads V_2 to V_3 (minor) would not be diagnosed as having RV dysplasia (three minor criteria). However, a patient with severe RV dilatation and dysfunction (major), frequent extrasystoles on monitoring (minor), and T-wave inversions in V_2 to V_3 (minor) would. Thus, the accurate characterization of the echo findings becomes crucial.

In this issue of the *Journal*, the article by Yoerger et al. (2) from the National Institutes of Health (NIH)-funded ARVD study makes important strides in clarifying the echocardiographic criteria. First, these investigators determined quantitative criteria for defining abnormal RV size and function. They found, for example, that diastolic dilation of the RV outflow tract in the parasternal long axis view (>30 mm) was the most common abnormality occurring in 100% of the probands. Second, they clarified the strength of abnormal RV morphology in establishing the diagnosis. For example, anterior RV wall-motion abnormalities were common (70%), abnormally prominent trabeculations were seen in the majority (54%), and sacculations were seen in 17%. None of the normal controls had these more specific findings.

Several points should be made in reference to this contribution. Firstly, the diagnosis was made on the basis of Task Force criteria independent of the echo findings in 28 of 29 patients. This is an eminently reasonable approach when trying to assess the value of echocardiographic findings but introduces a bias in the sense that the patients included may have had established disease, sufficiently advanced to be manifest using other morphologic criteria (presumably derived from RV angiography or cardiac magnetic resonance imaging [MRI]). The equally critical issue relative to the echocardiographic findings of ARVD in patients with mild disease is not addressed in this report.

Currently, three genetic mutations have been described as causes of 30% to 50% of patients with ARVD (3). These include mutations in genes that control cell-to-cell adhesion junctions (i.e., plakoglobin, desmoplakin, or plakophillin) or abnormalities in the ryanodine receptor. These genetic abnormalities allow investigators to precisely track development of ARVD. For example, in those with Naxos disease (plakoglobin mutation) (4), the disease phenotype does not appear until adolescence. In addition, sudden cardiac death has been reported in athletes who have very mild or inapparent structural abnormalities (5) and emphasizes the importance of detecting the subtle early findings.

The investigators found that dilation of the RV outflow tract (>30 mm) using the parasternal view was an excellent parameter for diagnosing ARVD in the appropriate setting. One of the most important confounding diagnoses that a clinician must distinguish from ARVD is that of RV outflow tract ventricular tachycardia. Others using MRI studies have found evidence of RV outflow dilation in patients with RV outflow tract ventricular tachycardia (6). The distinction between these two entities is very important since RV outflow tract ventricular tachycardia is usually benign and often responds to ablative therapy. It is hoped that further experience from the NIH study group will allow us to better distinguish these two diagnoses. The finding of diffuse global and/or major segmental RV abnormalities will clearly favor ARVD. However, the issue of presentation of the patient with less advanced disease still remains an important problem.

Another significant problem with the report by Yoerger et al. (2) is lack of correlative information vis-à-vis other invasive and non-invasive testing. This information was not presented because of the nature of the study protocol. Therefore, we avidly look forward to future reports where echocardiographic findings can be correlated with other abnormalities.

Finally, we hope the real value of the NIH studies is that they will ultimately provide for a large cohort of patients in

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whom the diagnosis of ARVD is more secure, either on the basis of cardiac histology (which is part of the registry protocol) (7), after prolonged follow-up observations, or with genetic testing. The correlation of existing data with a truer gold standard would be clearly an important advance.

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